REMARKS

An RCE is being contemporaneously filed to address the points raised in the Advisory Action. A revised Declaration is also attached.

The amendments to the claims incorporate the subject matter of claims 2 and 4 into the independent claims so as to address the Examiner's general objection to the overall breadth of the claims. The recitation of "at least" is deleted from claim 3 to more specifically direct attention to this aspect of Hypol PreMa G-50 which is a reaction product of PEG of a molecular weight of about 5500. No other additions are made to the claims.

It is submitted that amended claim 1 would not be obvious from the disclosure of U.S. Patent No. 5,624,711 to Sundberg et al. (hereinafter Sundberg et al.) in view of the disclosure U.S. Patent No. 5,169,720 to Braatz et al. (hereinafter Braatz et al.). Contrary to the Examiner's assertion in the Advisory Action, Sundberg et al. do not disclose a plurality of optically clear, three-dimensional hydrogel cells at least 20 microns thick at discrete locations on the surface of a solid substrate, which hydrogels are formed from an isocyanate-functional prepolymer with urethane linkages. The Examiner points to the character of the substrate, whereas the claim is directed to the discrete cells that are located on the surface of the substrate. In contrast to Applicants, Sundberg et al. use a derivatized solid surface that is covered with a uniform thin film of a polymeric resin material similar to the Merrifeld resins that have been used for decades for the solid-state synthesis of peptides and oligonucleotides. There is absolutely nothing three-dimensional about the Sundberg et al. array; it is clearly two-dimensional. It is a uniform, thin polymeric film, see column 15, line 31, and column 16, lines 51-52. The

coating is applied by dipping a glass slide in a solution of the polymer and evaporating the solvent. As shown in FIGS. 8 and 9, it is essentially a single molecular layer thick attached to the glass. It is uniform – there are no discrete cells, and certainly there are no discrete cells that are 20 microns thick.

Recognizing that Sundberg et al. does not utilize a three-dimensional hydrogel which is formed an isocyanate-functional prepolymer with urethane linkages, in which proteins and other immunoglobins are immobilized, the Examiner would cure this deficiency by combining the Sundberg et al. disclosure with that of Braatz et al. It is submitted that there is no teaching or suggestion in Braatz et al. that would lead one to make such a substitution of materials; in fact, Braatz et al. teaches away from such a substitution because, as its title clearly indicates, Braatz et al. is concerned with providing a "protein non-absorptive polymer coated device". Thus, the Examiner's *prima facie* case for obviousness fails.

As pointed out in the Abstract, Braatz et al. is concerned with providing a medical or laboratory device which is resistant to nonspecific protein absorption. Being filed together with this paper is a copy of a Declaration from one having ordinary skill in this art, who has worked in the field of microarrays for some six years, and who attests to the fact that the meaning of the term "nonspecific protein absorption" is well-known in the art as referring to the nonadherence of any and all proteins to the surface of a microarray substrate. As indicated by its title, this is the objective of Braatz et al.; they state in Examples XIII and XIV in column 18, that they are able to achieve resistance to all protein binding. There is simply no logical basis for the Examiner's assertion that "resistant to nonspecific protein absorption" implies that specific proteins can be absorbed. Proteins are all made of interlinked amino acids; thus, all proteins are simply

polypeptides. A coating that would generally resist protein absorption simply would not logically bind specific proteins which are simply a different rearrangement of the same 20 natural amino acids. This assertion is specifically addressed in paragraph 6 of the Declaration of Ms. Farideh Falcovitz-Gerassi, being filed with this paper.

It is submitted that it is illogical that one would look to the disclosure of a patent that teaches the formation of an overall coating that is designed to prevent any and all protein absorption/binding when one's desire is to provide a three-dimensional microcell upon and within which proteins and other binding agents can be immobilized. As a result, it is submitted that the Examiner's *prima facie* case of obviousness based upon the proposed combination of these two references must simply fail.

It is submitted that the invention as defined in amended claim 1 would likewise not be obvious from the disclosure of U.S. Patent No. 6,406,921 to Wagner et al. (hereinafter Wagner et al.) in view of Braatz et al. For the reasons set forth above, the primary deficiency lies in the teaching away of Braatz et al., and such is in no way cured by the disclosure of Wagner et al. Furthermore, Wagner et al. is similarly (to Sundberg et al.) deficient with respect to the teaching of three-dimensional, discrete cells at least about 20 microns thick; Wagner et al. even more specifically teaches a monolayer which comprises a linear hydrocarbon chain, one end of which is linked to the glass substrate surface and the other end of which includes a chemically active group that will bind to a protein or other binding agent. Wagner et al., at column 5, lines 56-57, define a monolayer as being a "single-molecule thick layer of organic molecules on a surface". At column 10, lines 10-11, Wagner et al. speak of their monolayer of molecules that is used to create patches used to attach the protein binding agents. Wagner et al. uses the term "monolayer" throughout the disclosure, see column 19, lines 4-5, 25, 47, and 59, as

well as in the titles to Examples II and IV. Moreover, Wagner et al. refer to their array as comprising two-dimensional patterns of proteins immobilized on these patches (see column 6, lines 61-63 and titles to Examples 1 and 2). Such a one-molecule thick layer is what is illustrated in the drawings of both Wagner et al. and Sundberg et al. These are not three-dimensional cells with a thickness measurement of 20 microns or more; they are single-molecule thick layers that would be measured in Angstroms. A micron equals 10,000 Angstroms. Both of the primary references are clearly concerned with two-dimensional patches, not three-dimensional cells and, of course, use thin films of different polymeric materials for the attachment of the binding entities, which in Wagner et al. are proteins.

In any rejection under 35 U.S.C. § 103, in proceedings before the USPTO, the Examiner bears the burden of establishing a *prima facie* case of obviousness based upon the prior art. The Examiner can satisfy this burden only by showing some objective teaching in the prior art that would lead an individual to combine the relevant teachings of the references. It is submitted that there is no objective teaching in Braatz et al., or in either of the other references which would suggest or motivate one to so alter the teaching of either Wagner et al. or Sundberg et al. to arrive at Applicants' claimed invention.

The Federal Circuit has often reiterated the manner in which obviousness rejections are to be reviewed. Where claimed subject matter has been rejected as obvious in view of a combination of prior art references, "a proper analysis under § 103 requires, *inter alia*, consideration of two factors: (1) whether the prior art would have suggested to those of ordinary skill in the art that they should make the claimed composition or device, or carry out the claimed process; and (2) whether the prior art would also have revealed

that in so making or carrying out, those of ordinary skill would have a reasonable expectation of success." *In re Vaeck*, 947 F.2d 488, 493, 20 U.S.P.Q.2d 1438, 1442 (Fed. Cir. 1991), citing *In re Dow Chemical Co.*, 837 F.2d 469, 473, 5 U.S.P.Q.2d 1529, 1531 (Fed Cir. 1988). The Federal Circuit emphasized this holding by succinctly summarizing: "Both the suggestion and the reasonable expectation of success must be founded in the prior art, not in the Applicants' disclosure" *Id.*

It is settled law that the combination of one reference with another is not proper unless there is some suggestion or motivation to make such a modification -- which may not be only in the hindsight of Applicants' disclosure. In this respect, the decision of the CAFC in the case of *In re Fritch*, 23 USPQ2d 1780, 1783 (Fed. Cir. 1992) is particularly pertinent:

> "Obviousness cannot be established by combining the teachings of the prior art to produce the claimed invention, absent some teaching or suggestion supporting the combination. Under section 103, teachings of references can be combined only if there is some suggestion or incentive to do so. *ACS Hosp. Systems, Inc. v. Montefiore Hosp.*, 732 F.2d 1572, 1577, 221 USPQ 929, 933 (Fed. Cir. 1984). Although couched in terms of combining teachings found in the prior art, the same inquiry must be carried out in the context of a purported obvious 'modification' of the prior art. The mere fact that the prior art may be modified in the manner suggested by the Examiner does not make the modification obvious unless the prior art suggested the desirability of the modification."

In summary, the Examiner has the burden to make a *prima facie* case of obviousness, and such a *prima facie* case requires teaching or suggestion which supports the combination in one of the prior art references. Absent such, the *prima facie* case fails. The Federal Circuit has stated that

> "...rejections on obviousness grounds cannot be sustained by mere conclusory statements; instead, there must be some articulated reasoning with some rational underpinning to support the legal conclusion of obviousness." *In re Kotzab*, 217 F.3d 1365, 1370 [55 USPQ2d 1313] (Fed. Cir. 2000).

In that decision, the Federal Court stated "Broad conclusory statements standing alone are not 'evidence'" *Id.* and held that:

> "In light of our holding of the absence of a motivation to combine the teachings in Evans, we conclude that the Board did not make out a proper *prima facie* case of obviousness...." *Id.*

It is submitted that the Examiner has not here made any such reasonable showing supported by articulated reasoning with rational underpinnings that one would be motivated to incorporate the 1992 teaching of Braatz et al. into the 1995 and 1998 teachings of Sundberg et al. and Wagner et al., and it is submitted such a showing cannot fairly be made. In conclusion, in addition to the failure of the *prima facie* case with respect to combination, neither of the primary references teaches discrete three-dimensional hydrogel cells at least 20 microns thick formed from an isocyanate-functional prepolymer with urethane linkages within or upon which binding entities are immobilized. Quite simply, the secondary reference to Braatz et al. does not fairly suggest the substitution of three-dimensional cells of a different material into the microarrays of either of those references, where the entire purpose of Braatz et al. is to teach coatings which are highly protein non-absorptive. Thus, it is respectfully requested that the rejections under 35 U.S.C. § 103 be reconsidered and withdrawn.

Independent claims 18 and 31 have been similarly amended to incorporate the subject matter of original claims 2 and 4. Claim 41 is likewise amended to specify that the three-dimensional discrete hydrogel cells are at least 20 microns thick. Accordingly, these three independent claims are submitted to be allowable for the same reasons as set forth with respect to amended claim 1. In summary, these four independent claims and dependent claims 3, 5-7, 9, 10, 16, 17, 32-35 and 42-43 should be allowed, and allowance

thereof is respectfully requested. Upon allowance of claim 1, it is submitted that claims 8 and 11-14, 36, and 38-40 to the non-elected species should be likewise allowed. As the Examiner noted, upon the allowance of a product claim, claims to the method of using the product, namely claims 44-45 should be examined, and examination and allowance of those two claims is further requested. In view of the foregoing amendments and remarks, it is believed that the application should now be in condition for allowance, and favorable action is courteously solicited.

Respectfully submitted,

Fitch, Even, Tabin & Flannery

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Attachment: Declaration Pursuant to 37 C.F.R. § 1.132 of Yehudit Falcovitz-Gerassi